

Hepatic Cryosurgery for Recurrent Hepatocellular Carcinoma After Hepatectomy: A Preliminary Report

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Background and Objectives: The treatment of choice for recurrent hepatocellular carcinoma (HCC) is repeated resection. However, only a small percentage of patients are suitable for further hepatic resection. The aim of this study was to evaluate the surgical risk and operative outcome of hepatic cryosurgery in patients with recurrent HCC.

Methods: A retrospective analysis of patients with recurrent HCC after previous curative hepatectomy treated with cryosurgery. Four patients with recurrent HCC not suitable for further resection were enrolled for cryosurgery, their clinical parameters, the operative details and outcome were studied.

Results: No intraoperative or postoperative complications were noted. The duration of operation ranged from 3–5.2 hr and the operative blood loss from 173–1,300 ml. All patients are still alive with survival after cryosurgery ranging from 12–23 mo (25–63 mo after the hepatic resection). Three patients showed evidence of recurrent disease and one patient was disease free.

Conclusions: Hepatic cryosurgery is a safe therapy for patients with unresectable recurrent HCC.

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KEY WORDS: hepatocellular carcinoma; recurrent hepatocellular carcinoma; cryosurgery; cryotherapy

INTRODUCTION

Hepatocellular carcinoma (HCC), a common disease in Asia, is the second most common cancer causing death in Hong Kong [1]. With the recent advances in diagnostic modality and surgical technology, more patients are suitable for hepatic resection [2]. However, the prognosis of patients with HCC remains poor because of the high incidence of recurrence. Intrahepatic recurrence after curative resection for HCC is the most significant cause of death. Only about 24% of the recurrent cases are suitable for repeated resection [3]. However, a repeat hepatectomy is technically difficult because of severe adhesions and anatomic alterations resulting from the previous operation [4]. It is also potentially risky because of the limited hepatic reserve [4].

In recent years, various local treatments like transarterial oily chemoembolization (TOCE), percutaneous

ethanol injection (PEI), microwave coagulation therapy, and laser therapy have been tried with different degrees of success. Hepatic cryosurgery has been advocated recently for the management of unresectable hepatocellular carcinoma [5] and hepatic metastases [6]. The aim of the present study was to evaluate the surgical risk and outcome of hepatic cryosurgery in patients with recurrent HCC after previous hepatectomy.

MATERIALS AND METHODS

All patients with histologically proven HCC after curative resection were followed up regularly with ultra-

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TABLE I. Clinical Parameters of Patients Who Received Cryosurgery for Recurrent Hepatocellular Carcinoma*

Case no.	Sex/Age	First operation	Liver status	Pattern of recurrence and size of tumour	Treatment received before cryosurgery
1	M/64	L hemihepatectomy	HBsAg related cirrhosis	solitary, 22 mm	nil
2	M/51	Extended R hemihepatectomy	HBsAg carrier	multiple, 38 mm, 5 mm, 5 mm	TOCE
3	M/63	L lateral segmentectomy	HBsAg related chronic active hepatitis	solitary 40 mm	TOCE
4	M/45	L hemihepatectomy	HBsAg related chronic active hepatitis	solitary, 60 mm	TOCE

*HBsAg: hepatitis B surface antigen; TOCE: transarterial oily chemoembolisation; L, left; R, right.

sound study, CT scan examination and serum α -fetoprotein concentration assay. Hepatic recurrence was diagnosed preoperatively with CT scan, hepatic arteriogram and serum α -fetoprotein concentration assay. Patients with hepatic disease only who were not suitable for further hepatic resection due to limited hepatic functional reserve were enrolled for cryosurgery.

Hepatic Cryosurgery

Hepatic cryosurgery was performed with the Cryotech LCS2000 unit (Cryogenic Technology, Derbyshire, UK) using a 3 or 5 mm diameter liquid nitrogen cryoprobe. The old incision was used in every case. Adhesions were taken down to adequately expose the liver. Intraoperative ultrasound was performed to locate the recurrent tumor and exclude the presence of additional tumors. A Tru-cut needle biopsy of the lesion was taken under ultrasonographic guidance for frozen section and hematoxylin and eosin staining. The implantation of the cryoprobe was guided by ultrasonography. The temperature recorded by the cryosurgical unit was kept at below -180°C during the freezing cycle. Freezing was complete when a margin of at least 1 cm normal hepatic tissue was frozen circumferentially around the tumour. The cryoprobe was held steadily until complete thawing took place around the cryoprobe. The tract formed was sealed off with fibrin glue immediately after removal of the cryoprobe to prevent hemorrhage.

Follow-up

All patients had CT scan examination within 1 mo after cryosurgery to exclude residual tumour. They were all followed up at monthly intervals. The serum α -fetoprotein concentration was assayed during each visit. A CT scan study of the liver was done every 3 mo in the initial 6 mo postoperatively and every 6 mo subsequently to detect recurrence.

RESULTS

Four male patients with recurrent HCC unsuitable for further resection received hepatic cryosurgery. Their clinical parameters are shown in Table I. All patients had

hepatitis B related liver diseases as shown from their resected liver in the first operation. Three patients had TOCE before cryosurgery, but they all failed to respond to the treatment. All hepatic recurrences were confirmed subsequently by histopathological study from tissue obtained during cryosurgery.

The total operative time ranged from 3–5.2 hr and the intraoperative blood loss from 170–1,300 ml (Table II). There was no intraoperative or postoperative complication identified. All patients had transient raise in the serum concentration of transaminases, which returned to normal within a week after cryosurgery. A transient thrombocytopenia was also uniformly observed, but no bleeding complication was seen. All patients were discharged on postoperative day 8, except one who was discharged on day 10 because of low grade fever after cryosurgery.

Four patients are still alive but three of them developed recurrent disease in the liver and two have additional metastases in the lung. One patient (#4), whose hepatic recurrence was 6 cm in diameter, had a small residual tumor inside the cryolesion indicating inadequate cryoablation. However, this patient was not given further cryosurgery because a pulmonary metastasis was found 2 mo after the cryosurgery. The duration of survival ranged from 12–23 mo after hepatic cryosurgery and 25–63 mo after hepatectomy.

DISCUSSION

Repeated hepatic resection in patients with recurrent HCC has been widely reported [2–4]. Although some investigators have reported a prolonged survival compared to other treatment modalities, no prospective and randomized studies have been done. Nevertheless, several long-term disease-free survivors after repeat resection have been reported. Therefore, repeat hepatectomy should be considered first in patients with recurrent HCC. However, >75% of patients are not suitable for repeat resection [3]. The use of TOCE in this group of patients has been advocated [7]. However, TOCE may not be feasible in these patients if the hepatic functional reserve is limited. Furthermore, TOCE is not expected to

TABLE II. Operative Outcome of Patients After Hepatic Cryosurgery

Case no.	Intraoperative blood loss ml	Duration of operation hr	Duration of hospital stay days	Survival from hepatectomy mo	Survival from cryosurgery mo	Survival status
1	173	3	10	63	14	Alive with no evidence of disease
2	1100	3.5	8	53	23	Alive with liver and lung recurrence
3	1300	5.2	8	58	12	Alive with liver recurrence
4	1000	4	8	25	13	Alive with liver and lung recurrence

have a therapeutic effect if the tumor is hypovascular. The three patients who received TOCE in the present series showed an increasing tumor volume despite more than three sessions of TOCE therapy.

Percutaneous ethanol injection is a good local treatment and can be performed in patients with poor hepatic function. However, PEI is generally thought to be ineffective in tumors >3 cm in diameter. Similarly, microwave coagulation therapy is also not recommended for tumor more than 3 cm in diameter.

Hepatic cryosurgery has recently become popular in the management of HCC and hepatic metastases. Hepatic cryosurgery carries certain advantages over other forms of treatment for liver tumors. First, the cellular destruction with cryosurgery is predictable. The growth of a hepatic cryolesion obeys known physical principles of thermal conduction. Therefore, precise destruction of the tumor tissue can be achieved with preservation of the surrounding normal liver tissue. This is important in patients with limited hepatic functional reserve as commonly seen in cirrhotic patients with HCC and in patients after previous hepatectomy. Second, multifocal disease involving more than one segment of liver can be treated individually, leaving enough functional parenchyma for survival. A disseminated type of recurrence accounts for 30% of HCC recurrence.

Hepatic cryosurgery for the management of recurrent HCC had been described by Dalton and Eisenberg [8] in one patient, although the clinical detail and outcome were not known. Zhou et al. [5] also included four patients with recurrent HCC treated by cryosurgery in his series of 60 patients. Two of the four patients survived for 8.2 yr and 7.3 yr after cryosurgery, whereas the remaining two patients survived for <1 yr. However, the long-term survival benefit of this approach is still uncertain as the number of patients treated by this method is still small [9].

The best freezing regimen for hepatic cryosurgery has not been defined. Although double-freeze cycles can achieve a greater hepatocellular injury than single-freeze cycle, the potential lethal complications of hepatic cryosurgery including a DIC-like syndrome and renal and hepatic failure may be increased both in incidence and severity [10]. Therefore, in this series of patients with

active hepatitis or cirrhosis and marginal hepatic functional reserve, a single-freeze cycle was used.

The adequacy of a frozen margin of 1 cm around the tumor as in surgical excision has not been studied. Although the edge of the cryolesion may not reach the cell-lethal temperature defined by using cellular suspension in an ex vivo environment, a delayed secondary cellular destruction caused by microvascular damages is well known and its effect could only be assessed by in vivo study. Therefore, in clinical practice, a frozen margin of at least 1 cm is advisable, but further study is needed to verify its adequacy.

Further, as hepatic cryosurgery requires laparotomy, it seems to be less attractive than other local treatment modalities. Nevertheless, hepatic cryosurgery appears to be a safe procedure and can provide another option of treatment especially in those patients with recurrent HCC not responding to TOCE and not suitable for PEI treatment. Further refinement of the technique such as using a laparoscopic approach or percutaneous method may improve its usefulness in the management of recurrent HCC.

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